Remarks

The Amendments

Claim 1 has been amended to recite "[a] chemically modified double stranded short interfering nucleic acid (siNA) molecule comprising a separate sense strand and antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides, wherein: each strand of the siNA molecule is about 18 to about 27 nucleotides in length; the antisense strand of the siNA molecule comprises about 18 to about 27 nucleotides that are complementary to human Amyloid Precursor Protein (APP) RNA comprising SEQ ID NO:1905; the sense strand is complementary to the antisense strand and comprises a portion of the APP RNA nucleotide sequence of about 18 to about 27 nucleotides; about 50 to 100 percent of the nucleotide positions in each of the sense and antisense strands of the siNA molecule are chemically modified; and about 50 to 100 percent of the purine nucleotides in one or both strands of the siNA molecule are 2'-O-methyl purine nucleotides and about 50 to 100 percent of the pyrimidine nucleotides in one or both strands of the siNA are 2'-deoxy-2'-fluoro pyrimidine nucleotides." Support for the amendments can be found in the specification at, *inter alia,* page 15, lines 20-30; page 36, lines 1-10; page 71, lines 16-31; and page 77, lines 21-27, and page 153, and Figures 4-5, Tables III and IV, and throughout the specification. Support for the amendment is also present in the priority applications. *See, e.g.,* U.S. Provisional patent application Nos. 60/363,124 (*see,* page 12; lines 1-15 and page 425), 60/409,293 (*see,* page 35, lines 9-29; page 19, lines 20-29; and page 20, lines 1-10) and 60/440,129 (*see,* page 12, lines 1-20).

Claims 14-21 and 30 have been amended to recite the term "strand" instead of region. Support for the amendment can be found at, *inter alia*, page 15, lines 20-30; page 24, lines 15-32; page 25, lines 1-15 and throughout the specification.

Claims 15 and 18 have been amended to recite the phrase "about 50 to 100 percent of the" pyrimidine nucleotides. Support for the amendment can be found in U.S. Provisional patent application No. 60/440,129 at, *inter alia,* page 12, lines 1-20 and throughout the specification.

Claim 19 has been amended to recite the phrase "about 50 to 100 percent of the" purine nucleotides. Support for the amendment can be found in the specification at, *inter alia*, page 15, lines 20-30; page 24, lines 15-32; page 25, lines 1-15, and throughout the specification.

Claims 14 and 20 have been amended to recite the phrase "one or more" purine nucleotides. Support for the amendment can be found in the specification at, *inter alia*, page 15, lines 20-30; page 24, lines 15-32; page 25, lines 1-15, and throughout the specification.

Claims 14, 18, and 19 have been amended to recite the phrase "present in." Support for the amendment can be found in the specification at, *inter alia*, page 15, lines 20-30; page 24, lines 15-32; page 25, lines 1-15, and throughout the specification.

Claims 21 and 30 have been amended to recite the term "terminal." Support for the amendment can be found in the specification at, *inter alia*, page 142, lines 15-30 and throughout the specification.

Claim 30 has been amended to recite "the siNA molecule of claim 1, wherein the said antisense strand includes a terminal phosphate group." Support for the amendment can be found in the specification at, *inter alia*, page 32, lines 1-15 and throughout the specification.

Claim 35 has been amended to recite "a composition comprising the siNA molecule of claim 1 in a pharmaceutically acceptable carrier or diluent." Support for the amendment can be found in the specification at, *inter alia*, page 59, lines 10-25, and throughout the specification.

Claims 2, 4-13, 22-29, and 31-34 have been canceled with this amendment without prejudice.

Amendments to the claims are made without prejudice and do not constitute amendments to overcome any prior art or other statutory rejections and are fully supported by the specification as filed. Additionally, these amendments are not an admission regarding the patentability of subject matter of the canceled or amended claims and should not be so construed. Applicant reserves the right to pursue the subject matter of the previously filed claims in this or in any other appropriate patent application. The amendments add no new matter and applicants respectfully request their entry.

The Sequence Listing

Applicants have enclosed a new sequence listing and request its entry in place of the previously entered sequence listing. The sequence listing adds SEQ ID NOs:1901-1905. SEQ ID NOs:1901-1904 identify duplex forming oligonucleotide, palindromic, or repeat sequences shown in original Figures 14 B-D. SEQ ID NO:1905 represents GenBank entry NM_000484 (*see*, page 153). The version of NM_000484 appearing in the sequence listing as SEQ ID NO:1905 appeared in GenBank on October 31, 2000 and is included in the U.S. Provisional patent application No. 60/363,124 priority application (*see,* page 425). The sequence listing adds no new matter and applicants respectfully request its entry.

The Restriction Requirement

The restriction requirement asserts that a restriction is necessary for claim 33 because the claim allegedly "contains sequences considered to be unrelated, since each siNA sequence claimed is

structurally and functionally independent and distinct" and thus is "not considered to be a proper genus/Markush group." Claim 33 has been canceled. As such the restriction requirement is moot. Additionally, none of the remaining claims recite more than one sequence. Therefore, it is the Applicants' good faith belief that an election is not necessary.

Conclusion

In view of the foregoing amendments and remarks, the applicant submits that the claims are in condition for allowance, which is respectfully solicited. If the examiner believes a teleconference will advance prosecution, she is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

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Date: 3/10/07

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